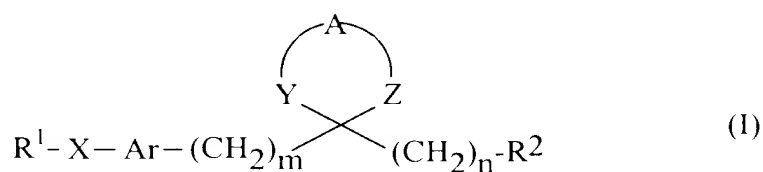


14. (Amended) A method for inhibiting matrix metalloproteinases (MMP) or tumor necrosis factor  $\alpha$  (TNF  $\alpha$ ), the method comprising administering to a patient an effective amount of the compound of Claim 1 or a pharmaceutically acceptable salt thereof.

15. (Amended) A process for manufacturing a medicament, said process comprising contacting the compound of Claim 1 or a pharmaceutically acceptable salt thereof with a pharmaceutically acceptable carrier.

Please add new claims 18-31.

18. (New) A compound of the formula:



in which  $\text{R}^1$  is lower alkyl, halogen, optionally substituted heterocyclic group or optionally substituted aryl,

$\text{R}^2$  is carboxy, protected carboxy or amidated carboxy,

Ar is thienyl,

A is ethylene or trimethylene,

X is oxa or a single bond,

Y is thia, sulfinyl or sulfonyl,

Z is methylene,

m and n are each an integer of 0 to 6, and

$$1 \leq m+n \leq 6,$$

and its salt.

19. (New) The compound of claim 18, in which the heterocyclic group of R<sup>1</sup> is selected from the group consisting of:

- (1) unsaturated 3- to 8-membered, heteromonocyclic group containing 1 to 4 nitrogen atoms,
- (2) saturated 3- to 8-membered, heteromonocyclic group containing 1 to 4 nitrogen atoms,
- (3) unsaturated 3- to 8-membered, heteromonocyclic group containing 1 or 2 sulfur atoms,
- (4) unsaturated condensed 7- to 13-membered, heterocyclic group containing 1 to 5 nitrogen atoms,
- (5) unsaturated 3- to 8-membered, heteromonocyclic group containing 1 or 2 oxygen atoms,
- (6) saturated 3- to 8-membered, heteromonocyclic group containing 1 or 2 oxygen atoms,
- (7) unsaturated 3- to 8-membered, heteromonocyclic group containing 1 or 2 oxygen atoms and 1 to 3 nitrogen atoms,
- (8) unsaturated condensed 7- to 13-membered, heterocyclic group containing 1 or 2 oxygen atoms,
- (9) unsaturated condensed 7- to 13-membered, heterocyclic group containing 1 or 2 sulfur atoms,
- (10) saturated 3- to 8-membered, heteromonocyclic group containing 1 or 2 oxygen atoms and 1 to 3 nitrogen atoms,
- (11) unsaturated condensed 7- to 13-membered, heterocyclic group containing 1 or 2 oxygen atoms and 1 to 3 nitrogen atoms,

- (12) unsaturated 3- to 8-membered, heteromonocyclic group containing 1 or 2 sulfur atoms and 1 to 3 nitrogen atoms,
- (13) saturated 3- to 8-membered, heteromonocyclic group containing 1 or 2 sulfur atoms and 1 to 3 nitrogen atoms, and
- (14) unsaturated condensed 7- to 13-membered, heterocyclic group containing 1 or 2 sulfur atoms and 1 to 3 nitrogen atoms, and

the aryl group of  $R^1$  is  $C_6$ - $C_{10}$  aryl, and further,

each of the above-mentioned heterocyclic group and aryl group are optionally substituted by a group selected from the group consisting of:

- (A1) halogen,
- (A2) lower alkyl,
- (A3) lower alkoxy,
- (A4) halo(lower)alkyl,
- (A5) halo(lower)alkoxy,
- (A6) lower alkenyl,
- (A7) acyl,
- (A8) lower alkylthio, lower alkylsulfinyl, lower alkylsulfonyl,
- (A9)  $C_6$ - $C_{10}$  aryl,
- (A10) halo( $C_6$ - $C_{10}$ )aryl,
- (A11) hydroxy,
- (A12) hydroxy(lower)alkyl, protected hydroxy(lower)alkyl,
- (A13) amino,
- (A14) carboxy,
- (A15) protected carboxy,

- (A16) nitro(lower)alkenyl,
- (A17) lower alkylendioxy,
- (A18) acylamino,
- (A19) nitro,
- (A20) (C<sub>6</sub>-C<sub>10</sub>)aryl(lower)alkoxy,
- (A21) carbamoyl(lower)alkenyl optionally N-substituted by the group consisting of  
lower alkyl, C<sub>6</sub>-C<sub>10</sub> aryl, lower alkoxy(C<sub>6</sub>-C<sub>10</sub>)-aryl, and halo(C<sub>6</sub>-C<sub>10</sub>)aryl,
- (A22) lower alkylaminocarbonyloxy,
- (A23) lower alkanoyloxy,
- (A24) lower alkoxy(lower)alkanoyloxy,
- (A25) lower alkoxy carbonyloxy,
- (A26) lower alkenoyloxy optionally substituted by heterocyclic group of the above  
(1) to (14),
- (A27) lower cycloalkanecarbonyloxy,
- (A28) lower alkoxy substituted by the group consisting of carboxy, protected  
carboxy, lower alkanoyl, lower cycloalkanecarbamoyl, and lower  
alkylcarbamoyl,
- (A29) lower alkylcarbamoyloxy(lower)alkyl,
- (A30) lower alkoxy carbonylamino(lower)alkyl,
- (A31) amino(lower)alkyl,
- (A32) lower alkylcarbamoyl(lower)alkyl,
- (A33) heterocyclic-carbonylamino, the heterocyclic group being selected from the  
above (1) to (14) and optionally being substituted N-protective group,

(A34) the above heterocyclic groups (1) to (14) being optionally substituted by lower alkyl, and

(A35) oxo.

20. (New) The compound of claim 19, in which

$R^1$  is lower alkyl, halogen, optionally substituted heterocyclic group, or aryl selected from the group consisting of phenyl and naphthyl;

$R^2$  is carboxy, lower alkoxy carbonyl, hydroxyaminocarbonyl, tetrahydropyranyloxyaminocarbonyl, or phenyl(lower)alkylaminocarbonyl, and

m and n are each an integer of 0 or 1, and  $m+n=1$  or 2,

wherein the heterocyclic group is selected from the group consisting of:

- (1) unsaturated 5- or 6-membered heteromonocyclic group containing 1 to 4 nitrogen atoms,
- (2) saturated 5- or 6-membered, heteromonocyclic group containing 1 to 4 nitrogen atoms,
- (3) unsaturated 5- or 6-membered heteromonocyclic group containing 1 to 2 sulfur atoms,
- (4) unsaturated bicyclic 9- or 10-membered, heterocyclic group containing 1 to 5 nitrogen atoms,
- (5) unsaturated 5- or 6-membered heteromonocyclic group containing 1 to 2 oxygen atoms,
- (6) saturated 5- or 6-membered, heteromonocyclic group containing 1 or 2 oxygen atoms,
- (7) unsaturated 5- or 6-membered, heteromonocyclic group containing 1 or 2 oxygen atoms and 1 to 3 nitrogen atoms,

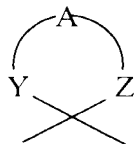
- (8) unsaturated bicyclic 9- or 10-membered, heterocyclic group containing 1 or 2 oxygen atoms,
- (9) unsaturated bicyclic 9- or 10-membered, heterocyclic group containing 1 or 2 sulfur atoms, or
- (10) saturated 5- or 6-membered, heteromonocyclic group containing 1 or 2 oxygen atoms and 1 to 3 nitrogen atoms,

wherein the heterocyclic group being optionally substituted by a group selected from the group consisting of the following (B1) to (B8):

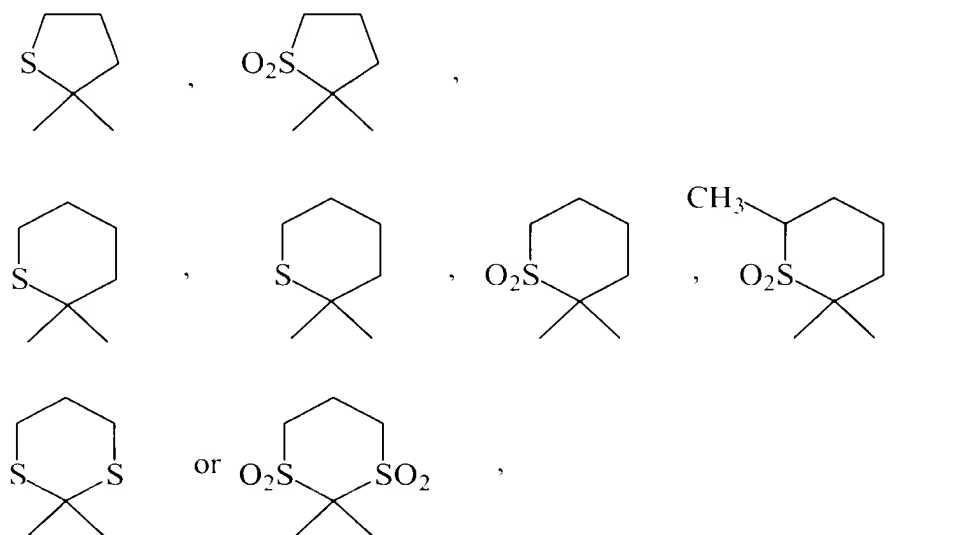
- (B1) lower alkanoyl,
- (B2) lower alkyl,
- (B3) lower alkoxy,
- (B4) lower alkoxycarbonylamino,
- (B5) carbamoyl or lower alkylcarbamoyl,
- (B6) lower alkoxycarbonyl,
- (B7) halo, and
- (B8) oxo;

and the aryl is optionally substituted by a group selected from the group consisting of (A1) to (A35) as defined in claim 19.

21. (New) The compound of claim 20, in which  
a group of the formula:



is one of the following formulae:



$R^1$  is lower alkyl, halogen, optionally substituted heterocyclic group or aryl selected from the group consisting of phenyl and naphthyl;

$R^2$  is carboxy, lower alkoxy, hydroxyaminocarbonyl, or tetrahydropyranyloxyaminocarbonyl, and

$m$  and  $n$  are each an integer of 0 or 1, and  $m+n=1$  or 2,

wherein the above-mentioned heterocyclic group is

- (1) pyrrolyl, pyrrolinyl, imidazolyl, pyrazolyl, pyridyl, pyridyl N-oxide, pyrimidyl, pyrazinyl, pyridazinyl, triazolyl, tetrazolyl, dihydrotriazinyl,
- (2) azetidiny, pyrrolidinyl, imidazolidinyl, piperidinyl, piperidino, pyrazolidinyl, piperazinyl,
- (3) thienyl,

- (4) indolyl, isoindolyl, indolizinyl, benzimidazolyl, quinolyl, isoquinolyl, tetrahydroisoquinolyl, indazolyl, benzotriazolyl, tetrazolopyridyl, tetrazolopyridazinyl, dihydrotriazolopyridazinyl,
- (5) furyl,
- (6) oxolanyl,
- (7) oxazolyl, isoxazolyl, oxadiazolyl,
- (8) benzofuranyl, benzodihydrofuranyl, benzodioxolenyl,
- (9) benzothienyl, dihydrobenzothienyl,
- (10) morpholinyl, morpholino,

wherein the heterocyclic group being optionally substituted by a group selected from the group consisting of (B1) to (B8) as defined in claim 20,

and the aryl is optionally substituted by a group selected from the group consisting of the following (A1) to (A34):

- (A1) halogen,
- (A2) lower alkyl,
- (A3) lower alkoxy,
- (A4) halo(lower)alkyl,
- (A5) halo(lower)alkoxy,
- (A6) lower alkenyl,
- (A7) acyl,
- (A8) lower alkylthio, lower alkylsulfinyl, lower alkylsulfonyl,
- (A9) C<sub>6</sub>-C<sub>10</sub> aryl
- (A10) halo(C<sub>6</sub>-C<sub>10</sub>)aryl,
- (A11) hydroxy,

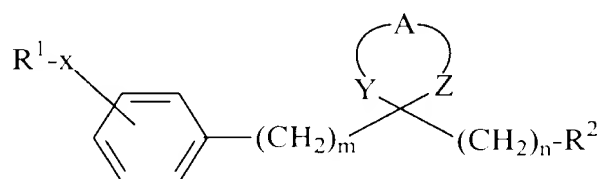


- (A12) hydroxy(lower)alkyl or protected hydroxy(lower)alkyl,
- (A13) amino,
- (A14) carboxy,
- (A15) protected carboxy,
- (A16) nitro(lower)alkenyl,
- (A17) lower alkylenedioxy,
- (A18) acylamino,
- (A19) nitro,
- (A20) (C<sub>6</sub>-C<sub>10</sub>)aryl(lower)alkoxy,
- (A21) carbamoyl(lower)alkenyl optionally N-substituted by the group consisting of  
lower alkyl, (C<sub>6</sub>-C<sub>10</sub>)aryl, lower alkoxy(C<sub>6</sub>-C<sub>10</sub>)-aryl, and halo(C<sub>6</sub>-C<sub>10</sub>)aryl,
- (A22) lower alkylaminocarbonyloxy,
- (A23) lower alkanoyloxy,
- (A24) lower alkoxy(lower)alkanoyloxy,
- (A25) lower alkoxycarbonyloxy,
- (A26) lower alkenoyloxy optionally substituted by the above heterocyclic group (1),
- (A27) lower cycloalkanecarbonyloxy,
- (A28) lower alkoxy substituted by the group consisting of carboxy, protected  
carboxy, lower alkanoyl, lower cycloalkanecarbamoyl, and lower  
alkylcarbamoyl,
- (A29) lower alkylcarbamoyloxy(lower)alkyl,
- (A30) lower alkoxycarbonylamino(lower)alkyl,
- (A31) amino(lower)alkyl,
- (A32) lower alkylcarbamoyl(lower)alkyl,

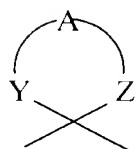
(A33) heterocyclic-carbonylamino, the heterocyclic group being selected from the above (2), (4) and (5) and optionally substituted by N-protective group, and

(A34) the heterocyclic group of the above (7) being optionally substituted by lower alkyl.

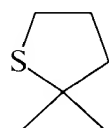
22. (New) The compound of claim 21, having the following formula:



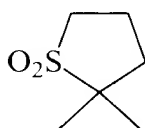
wherein a group of the formula:



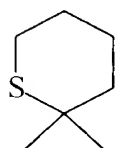
is one of the following formulae:



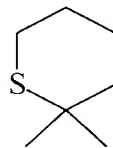
,



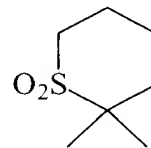
,



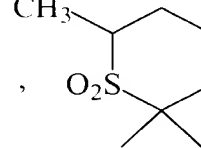
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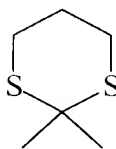
,



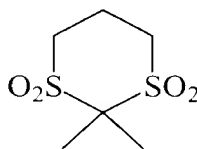
$CH_3$



,



or



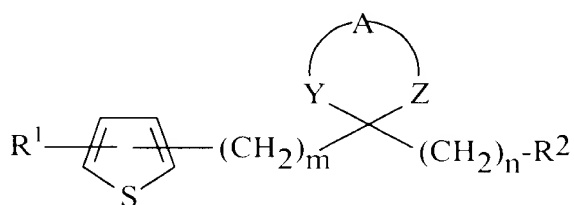
,

$R^1$  is lower alkyl, phenyl, halophenyl, or (halo)(phenyl)phenyl,

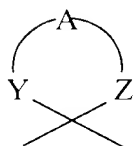
$R^2$  is carboxy or hydroxyaminocarbonyl, and

$m$  and  $n$  are each an integer of 0 or 1, and  $m+n=1$ .

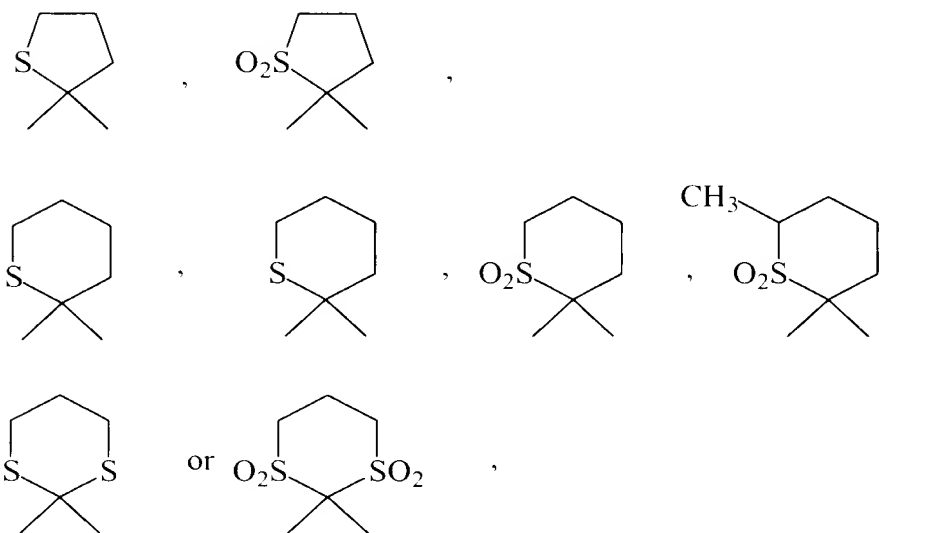
23. (New) The compound of claim 21, having the following formula:



wherein a group of the formula:



is one of the following formulae:



$R^2$  is carboxy or hydroxyaminocarbonyl,

m and n are each an integer of 0 or 1, and  $m+n=1$ ,

$R^1$  is halogen, heterocyclic group selected from the group consisting of pyridyl, thienyl, furyl, benzofuranyl or benzothienyl, wherein the heterocyclic group is optionally substituted by a group selected from the group consisting of lower alkanoyl, lower alkyl, lower alkoxy, lower alkoxycarbonylamino and lower alkylcarbamoyl; naphthyl or phenyl optionally substituted by a group selected from the group consisting of the following (C1) to (C31):

(C1) halogen,

(C2) lower alkyl,

(C3) lower alkoxy,

(C4) halo(lower)alkyl,

(C5) halo(lower)alkoxy,

(C6) lower alkenyl,

(C7) lower alkylcarbamoyl, carbamoyl, phenyl(lower)alkylcarbamoyl, lower alkanoyl,

(C8) lower alkylthio, lower alkylsulfinyl, lower alkylsulfonyl,

(C9) phenyl, naphthyl,

(C10) halophenyl,

(C11) hydroxy,

(C12) mono- or dihydroxy(lower)alkyl, phenoxycarbonyloxy(lower)alkyl

(C13) amino,

(C14) carboxy,

(C15) lower alkylendioxy,

(C16) lower alkanoylamino,

phenyl(lower)alkanoylamino, halophenyl(lower)alkanoylamino,

lower alkoxy(lower)alkanoylamino,

phenoxy(lower)alkanoylamino, lower alkoxyphenoxy(lower)alkanoylamino,

lower alkylphenoxy(lower)alkanoylamino,

halophenoxy(lower)alkanoylamino,

carboxy(lower)alkanoylamino, lower alkoxycarbonyl(lower)alkanoylamino,

lower alkylcarbamoyl(lower)alkanoylamino,

halo(lower)alkanoylamino,

lower alkenyl(lower)alkanoylamino,

lower alkoxy(lower)alkanoylamino,

phenyl(lower)alkoxy(lower)alkanoylamino,

piperidinyloxy(lower)alkanoylamino, N-lower alkoxycarbonylpiperidinyloxy-

lower)alkanoylamino, pyridyloxy(lower)alkanoylamino,

hydroxy(lower)alkanoylamino,

lower alkanoyloxy(lower)alkanoylamino,

lower alkylcarbamoyloxy(lower)alkanoylamino, N,N-di(lower  
alkyl)carbamoyloxy,

piperidino-carbonyloxy(lower)alkanoylamino,

phenyl(lower)alkylcarbamoyloxy(lower)alkanoylamino, lower

alkoxycarbonylamino(lower)alkanoylamino,

amino(lower)alkanoylamino, fluorenylmethoxycarbonylamino(lower)-  
alkanoylamino,

lower alkylamino(lower)alkanoylamino, [N,N-di(lower  
alkyl)amino](lower)alkanoylamino,  
[N-lower alkyl-N-(lower alkoxy carbonyl)-amino](lower)alkanoylamino, [N-  
lower alkyl-N-(fluorenylmethoxycarbonyl)amino](lower)alkanoylamino,  
[N-lower alkyl-N-(mono- or di(lower)-  
alkylcarbamoyl)amino](lower)alkanoylamino,  
[N-(mono- or di(lower alkyl)carbamoyl)amino](lower)alkanoylamino,  
benzoylamino(lower)alkanoylamino, lower  
alkanoylamino(lower)alkanoylamino, lower  
alkanesulfonylamino(lower)alkanoylamino,  
lower alkoxy(lower)alkanoylamino(lower)alkanoylamino,  
cyclo(lower)alkyloxycarbonylamino-(lower)alkanoylamino,  
pyridylcarbonylamino(lower)alkanoylamino,  
morpholinocarbonylamino(lower)alkanoylamino,  
phenyl(lower)alkoxyoxycarbonylamino(lower)alkanoylamino,  
lower alkoxyphenylsulfonylamino(lower)alkanoylamino,  
hydroxy(lower)alkylamino(lower)alkanoylamino,  
morpholino(lower)alkanoylamino, oxooxazolidinyl(lower)alkanoylamino,  
oxopyrrolidinyl(lower)alkanoylamino,  
trimethylhydantoinyl(lower)alkanoylamino,  
lower alkenylamino(lower)alkanoylamino,  
lower alkoxy(lower)alkylamino(lower)alkanoylamino,  
phenyl(lower)alkylamino(lower)alkanoylamino,  
pyridyl(lower)alkylamino(lower)alkanoylamino,

lower alkoxycarbonylamino, phenyl(lower)alkoxycarbonylamino,  
lower alkoxy(lower)alkoxycarbonylamino,  
halo(lower)alkoxycarbonylamino,  
amino(lower)alkoxycarbonylamino, phthalimido(lower)alkoxycarbonylamino,  
carbamoylamino,  
(mono- or di(lower alkyl)carbamoylamino,  
naphthylcarbamoylamino,  
halophenylcarbamoylamino,  
lower alkoxyphenylcarbamoylamino,  
lower alkenylcarbamoylamino,  
cyclo(lower)alkyl(lower)alkylcarbamoylamino,  
phenyl(lower)alkylcarbamoylamino,  
halo(lower)alkylcarbamoylamino,  
lower alkoxy(lower)alkylcarbamoylamino,  
hydroxy(lower)alkylcarbamoylamino, (lower  
alkyl)(diphenyl)silyloxy(lower)alkylcarbamoylamino,  
carboxy(lower)alkylcarbamoylamino, lower  
alkoxycarbonyl(lower)alkylcarbamoylamino,  
lower alkylcarbamoyl(lower)alkylcarbamoylamino, or  
pyridylcarbamoylamino,  
lower alkylsulfonylamino,  
lower alkenoylamino,  
lower cycloalkanecarbonylamino,  
lower alkenyloxycarbonylamino,

- phenoxycarbonylamino,
- lower alkylthiocarbonylamino,
- (C17) phenyl(lower)alkoxy,
- (C18) lower alkenyl, mono- or di(lower alkyl)carbamoyl(lower)alkenyl, (2-(methylcarbamoyl)ethenyl, 2-(ethylcarbamoyl)ethenyl, 2-(propylcarbamoyl)ethenyl, 2-(isopropylcarbamoyl)ethenyl, 2-(dimethylcarbamoyl)ethenyl,)
- phenylcarbamoyl(lower)alkenyl,
- lower alkoxycarbamoyl(lower)alkenyl,
- halophenylcarbamoyl(lower)alkenyl,
- (C19) lower alkylaminocarbonyloxy,
- (C20) lower alkanoyloxy,
- (C21) lower alkoxy(lower)alkanoyloxy,
- (C22) lower alkoxycarbonyloxy,
- (C23) pyridyl(lower)alkenoyloxy
- (C24) lower cycloalkanecarbonyloxy,
- (C25) carboxy(lower)alkoxy,
- lower alkoxycarbonyl(lower)alkoxy,
- lower alkanoyl(lower)alkoxy,
- lower cycloalkanecarbamoyl(lower)alkoxy,
- lower alkylcarbamoyl(lower)alkoxy,
- (C26) lower alkylcarbamoyloxy(lower)alkyl,
- (C27) lower alkoxycarbonylamino(lower)alkyl,
- (C28) amino(lower)alkyl,

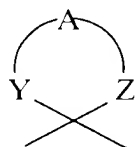


(C29) lower alkylcarbamoyl(lower)alkyl,

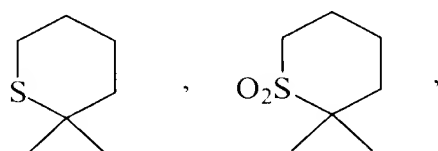
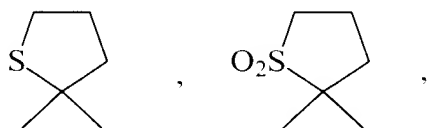
(C30) furylcarbonylamino, teretahydroisoquinolylcarbonylamino, N-lower  
alkoxycarbonyl-teretahydroisoquinolylcarbonylamino,  
pyrrolidinylcarbonylamino,

(C31) oxazolyl, lower alkyloxadiazolyl.

24. (New) The compound of claim 23, in which a group of the formula:

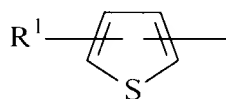


is one of the following formulae:



$R^2$  is hydroxyaminocarbonyl,

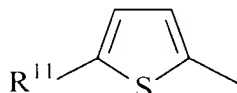
m is 0 and n is 1,



a group of the formula:

is a group selected from the group of the following formulae (a) to (e);

(a)

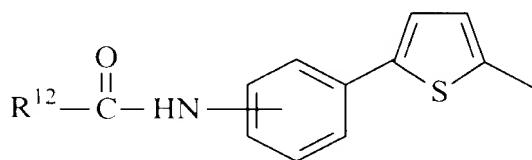


wherein

R<sup>11</sup> is halo, naphthyl, phenyl, mono- or dihalophenyl, mono- or di(lower)alkylphenyl, lower alkoxyphenyl, trihalo(lower)alkylphenyl, trihalo(lower)alkoxyphenyl, lower alkenylphenyl, lower alkylcarbamoylphenyl, carbamoylphenyl, phenyl(lower)alkylcarbamoylphenyl, lower alkanoylphenyl, lower alkylthiophenyl, lower alkylsulfinylphenyl, lower alkylsulfonylphenyl, phenylphenyl, (halo)(phenyl)phenyl, halophenylphenyl, hydroxyphenyl, mono- or dihydroxy(lower)alkylphenyl, phenoxycarbonyloxy(lower)alkylphenyl, aminophenyl, carboxyphenyl, lower alkylendioxyphenyl, lower alkanesulfonylaminophenyl, lower alkenoylaminophenyl, lower cycloalkanecarbonylaminophenyl, phenyl(lower)alkoxyphenyl, mono- or di(lower alkyl)carbamoyl(lower)alkenylphenyl, phenylcarbamoyl(lower)alkenylphenyl, lower alkoxy carbamoyl(lower)alkenylphenyl, halophenylcarbamoyl(lower)alkenylphenyl, lower alkylcarbamoyloxyphenyl, lower alkanoyloxyphenyl, lower alkoxy(lower)alkanoyloxyphenyl, lower alkoxy carbonyloxyphenyl, pyridyl(lower)alkanoyloxyphenyl, cyclo(lower)alkylcarbonyloxyphenyl, carboxy(lower)alkoxyphenyl, lower

alkoxycarbonyl(lower)alkoxyphenyl, lower alkanoyl(lower)alkoxyphenyl,  
 lower cycloalkanecarbamoyl(lower)alkoxyphenyl, lower  
 alkylcarbamoyl(lower)alkoxyphenyl, lower  
 alkylcarbamoxy(lower)alkylphenyl, lower  
 alkoxycarbonylamino(lower)alkylphenyl, amino(lower)alkylphenyl, lower  
 alkylcarbamoyl(lower)alkylphenyl, furylcarbonylamino-phenyl,  
 1,2,3,4-tetrahydroisoquinolylcarbonylamino-phenyl, N-t-butoxycarbonyl,  
 1,2,3,4-tetrahydroisoquinolylcarbonylamino-phenyl,  
 pyrrolidinylcarbonylamino-phenyl, oxazolylphenyl, lower  
 alkyloxadiazolylphenyl.

(b)



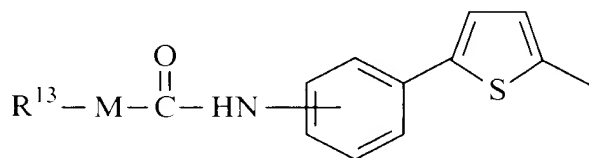
wherein

R<sup>12</sup> is lower alkyl optionally substituted by the group

consisting of phenyl, halophenyl, lower alkoxyphenyl, lower alkoxy, phenoxy,  
 lower alkoxyphenoxy, halophenoxy, lower alkylphenoxy, carboxy, lower  
 alkoxycarbonyl, lower alkylcarbamoyl, halo, lower alkenyloxy, lower  
 alkoxy(lower)alkoxy, phenyl(lower)alkoxy, piperidinyloxy, N-lower  
 alkoxycarbonyl-piperidinyloxy, pyridyloxy, hydroxy, lower alkanoyloxy,  
 mono- or di(lower)alkylcarbamoxyloxy, piperidinylcarbonyloxy,  
 phenyl(lower)alkylcarbamoxyloxy, lower alkoxycarbonylamino, amino,

fluorenylmethoxycarbonylamino, mono- or di(lower)alkylamino, N-lower alkyl-N-(lower alkoxy(alkoxycarbonyl)amino, N-lower alkyl-N-(fluorenylmethoxycarbonyl)amino, N-lower alkyl-N-(mono- or di(lower)alkylcarbamoyl)amino, N-(mono- or di(lower alkyl)carbamoyl)amino, benzoylamino, lower alkanoylamino, lower alkanesulfonylamino, lower alkoxy(lower)alkanoylamino, cyclo(lower)alkyloxycarbonylamino, pyridylcarbonylamino, morpholinocarbonylamino, phenyl(lower)alkoxy(alkoxycarbonyl)amino, lower alkoxyphenylsulfonylamino, hydroxy(lower)alkylamino, morpholino, oxooxazolidinyl, oxopyrrolidinyl, trimethylhydantoinyl, pyridyl, lower alkenylamino, lower alkoxy(lower)alkylamino, phenyl(lower)alkylamino, pyridyl(lower)alkylamino, and cyclo(lower)alkyl,

(c)



wherein

M is oxygen or sulfur,

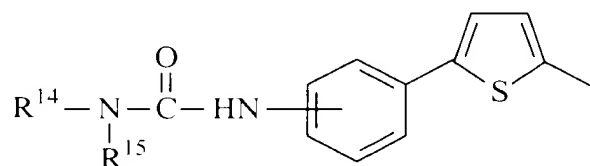
$R^{13}$  is lower alkyl, phenyl(lower)alkyl,

lower alkoxy(lower)alkyl, halo(lower)alkyl, amino(lower)alkyl, or

phthalimido(lower)alkoxy(alkoxycarbonyl)amino,

lower alkenyl, phenyl,

(d)

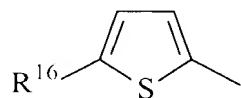


wherein

$R^{15}$  is hydrogen or lower alkyl,

$R^{14}$  is hydrogen, lower alkyl, naphthyl, halophenyl, lower alkoxyphenyl, lower alkenyl, lower cycloalkyl(lower)alkyl, phenyl(lower)alkyl, halo(lower)alkyl, lower alkoxy(lower)alkyl, hydroxy(lower)alkyl, (lower alkyl)(diphenyl)silyloxy(lower)alkyl, carboxy(lower)alkyl, lower alkoxy carbonyl(lower)alkyl, lower alkyl carbamoyl(lower)alkyl, or pyridyl,

(e)

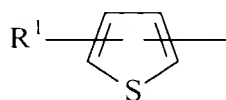


wherein

$R^{16}$  is benzothieryl, benzofuranyl, thienyl, furyl, lower alkylpyridyl, pyridyl, lower alkoxy pyridyl, lower alkoxy carbonylaminopyridyl, lower alkanoylthienyl, lower alkyl carbamoylbenzofuranyl.

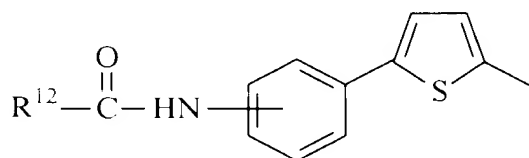
25. (New) The compound of claim 24, wherein

a group of the formula:



is the same group as (a), (c), (d) and (e) of claim 24, and the following formula (b):

(b)



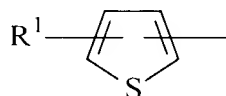
wherein

$R^{12}$  is lower alkyl, phenyl(lower)alkyl, halophenyl(lower)alkyl,  
lower alkoxyphenyl(lower)alkyl,  
lower alkoxy(lower)alkyl, phenoxy(lower)alkyl, lower  
alkoxyphenoxy(lower)alkyl, halophenoxy(lower)alkyl,  
lower alkylphenoxy(lower)alkyl, carboxy(lower)alkyl,  
lower alkoxy carbonyl(lower)alkyl,  
lower alkyl carbamoyl(lower)alkyl, halo(lower)alkyl, lower  
alkenyloxy(lower)alkyl, lower alkoxy(lower)alkoxy(lower)alkyl,  
phenyl(lower)alkoxy(lower)alkyl, piperidinyloxy(lower)alkyl,  
N-t-butoxycarbonylpiperidinyloxy(lower)alkyl, pyridyloxy(lower)alkyl,  
hydroxy(lower)alkyl,  
lower alkanoyloxy(lower)alkyl,

mono- or di(lower)alkylcarbamoyloxy(lower)alkyl,  
piperidinylcarbonyloxy(lower)alkyl,  
phenyl(lower)alkylcarbamoyloxy(lower)alkyl,  
amino(lower)alkyl,  
lower alkoxy-carbonylamino(lower)alkyl,  
fluorenylmethoxycarbonylamino(lower)alkyl,  
mono- or di(lower)alkylamino(lower)alkyl,  
N-lower alkyl-N-(lower alkoxy-carbonyl)amino(lower)alkyl,  
N-lower alkyl-N-(fluorenylmethoxycarbonyl)amino-  
(lower)alkyl, N-lower alkyl-N-(mono- or di(lower)-  
alkylcarbamoyl)amino(lower)alkyl, N-(mono- or di(lower alkyl)carbamoyl)-  
amino(lower)alkyl, benzoylamino(lower)alkyl,  
lower alkanoylamino(lower)alkyl,  
lower alkanesulfonylamino(lower)alkyl,  
lower alkoxy(lower)alkanoylamino(lower)alkyl,  
cyclo(lower)alkyloxycarbonylamino(lower)alkyl,  
pyridylcarbonylamino(lower)alkyl, morpholinocarbonylamino(lower)alkyl,  
phenyl(lower)alkoxyoxycarbonylamino(lower)alkyl,  
lower alkoxyphenylsulfonylamino(lower)alkyl,  
hydroxy(lower)alkylamino(lower)alkyl, morpholino(lower)alkyl,  
oxooxazolidinyl(lower)alkyl, oxopyrrolidinyl(lower)alkyl,  
trimethylhydantoinyl(lower)alkyl, pyridyl(lower)alkyl, lower  
alkenylamino(lower)alkyl, lower alkoxy(lower)alkylamino(lower)alkyl,

phenyl(lower)alkylamino(lower)alkyl, pyridyl(lower)alkylamino(lower)alkyl, cyclo(lower)alkyl, (amino)(phenyl)(lower)alkylamino, (lower alkoxycarbonylamino)(phenyl)(lower)alkyl, (amino)(lower alkoxy)-(lower)alkyl, (lower alkoxycarbonylamino)(lower alkoxy)(lower)alkyl, (amino)(carboxy)(lower)alkyl, (lower alkoxycarbonylamino)(carboxy)-(lower)alkyl, (amino)(lower alkoxycarbonyl)(lower)alkyl, (lower alkoxycarbonylamino)(lower alkoxycarbonyl)(lower)alkyl, (amino)(phenyl(lower)alkoxy)(lower)alkyl, (lower alkoxycarbonylamino)-(phenyl(lower)alkoxy)(lower)alkyl, (amino)(pyridyl)(lower)alkyl, (lower alkoxycarbonylamino)(pyridyl)(lower)alkyl, (amino)(hydroxy)-(lower)alkyl, (lower alkoxycarbonylamino)(hydroxy)(lower)alkyl, (amino)(amino)(lower)alkyl, (lower alkoxycarbonylamino)(amino)(lower)alkyl, (amino)(lower alkoxycarbonylamino)(lower)alkyl, (lower alkoxycarbonylamino)(lower alkoxycarbonylamino)(lower)alkyl, (amino)(lower cycloalkane)(lower)alkyl, (lower alkoxycarbonylamino)(lower cycloalkane)(lower)alkyl.

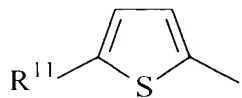
26. (New) The compound of claim 24, in which a group of the formula:



is a group selected from the group of the following formula (a) to (e):



(a)



wherein

R<sup>11</sup> is bromo, 2-naphthyl, phenyl,

3(or 4)-chlorophenyl, 2(or 3 or 4)-fluorophenyl, 3,4-dichlorophenyl, 3,5-difluorophenyl,

3(or 4)-methylphenyl, 4-ethylphenyl,

4-isopropylphenyl, 4-(t-butyl)phenyl,

3,4-dimethylphenyl, 4-methoxyphenyl,

4-ethoxyphenyl, 4-trifluoromethylphenyl,

4-trifluoromethoxyphenyl, 4-ethenylphenyl,

4-methylcarbamoylphenyl, 4-ethylcarbamoylphenyl, 4-carbamoylphenyl, 4-benzylcarbamoylphenyl,

4-acetylphenyl, 4-methylthiophenyl,

4-ethylthiophenyl, 4-methylsulfinylphenyl,

4-methylsulfonylphenyl, phenylphenyl, 4-phenyl-3-fluorophenyl,

4-(4-fluorophenyl)phenyl, 3(or 4)-hydroxyphenyl, 3(or

4)-hydroxymethylphenyl,

4-(1,2-dihydroxyethyl)phenyl,

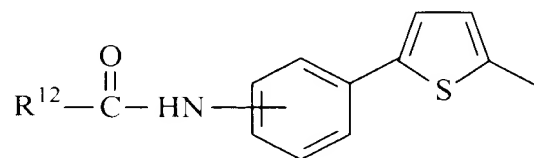
4-(phenoxycarbonyloxymethyl)phenyl, 3(or 4)-aminophenyl,

4-carboxyphenyl,

3,4-methylenedioxyphenyl,  
4-(methanesulfonylamino)phenyl,  
3-(2-butenoylamino)phenyl,  
3-(cyclopropanecarbonylamino)phenyl,  
3-(cyclobutanecarbonylamino)phenyl,  
3-(cyclopentanecarbonylamino)phenyl,  
4-benzyloxyphenyl,  
4-(2-(methylcarbamoyl)ethenyl)phenyl,  
4-(2-(ethylcarbamoyl)ethenyl)phenyl,  
4-(2-(propylcarbamoyl)ethenyl)phenyl,  
4-(2-(isopropylcarbamoyl)ethenyl)phenyl,  
4-2-(dimethylcarbamoyl)ethenyl)phenyl,  
4-(2-(phenylcarbamoyl)ethenyl)phenyl,  
4-(2-(methoxyphenylcarbamoyl)ethenyl)phenyl,  
4-(2-(4-fluorophenylcarbamoyl)ethenyl)phenyl,  
4-(methylaminocarbonyloxy)phenyl,  
4-(ethylaminocarbonyloxy)phenyl,  
4-propanoyloxyphenyl, 4-(methoxyacetyloxy)phenyl, 4-  
(ethoxycarbonyloxy)phenyl,  
4-(3-(3-pyridyl)acryloyloxy)phenyl,  
4-(cyclopropylcarbonyloxy)phenyl,  
4-(carboxymethoxy)phenyl,  
4-(ethoxycarbonylmethoxy)phenyl,  
4-(t-butoxycarbonylmethoxy)phenyl,

4-(propanoylmethoxy)phenyl,  
 4-(cyclopropylcarbamoylmethoxy)phenyl,  
 3(or 4)-(methylcarbamoylmethoxy)phenyl,  
 4-(ethylcarbamoylmethoxy)phenyl,  
 4-(propylcarbamoylmethoxy)phenyl,  
 3(or 4)-(methylcarbamoyloxymethyl)phenyl,  
 4-(methoxycarbonylaminomethyl)phenyl,  
 4-(t-butoxycarbonylaminomethyl)phenyl,  
 4-aminomethylphenyl,  
 4-(methylcarbamoylmethyl)phenyl,  
 3-(2(or 3)-furylcarbonylamino)phenyl,  
 3-(1,2,3,4-teretahydroisoquinolylcarbonylamino)phenyl,  
 3-(N-(t-butoxycarbonyl)-1,2,3,4-  
 teretahydroisoquinolylcarbonylamino)phenyl,  
 3-(pyrrolidinylcarbonylamino)phenyl,  
 4-(1,3-oxazolyl)phenyl,  
 4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl,

(b)



wherein

R<sup>12</sup> is methyl, ethyl, propyl, isopropyl, butyl, isobutyl, t-butyl, neopentyl,

phenylmethyl,

4-chlorophenylmethyl, 4-methoxyphenylmethyl,

methoxymethyl, ethoxymethyl, propoxymethyl, butoxymethyl,

isopropylloxymethyl, 1-methoxyethyl, 2-methoxyethyl, phenoxymethyl, 2-

phenoxyethyl, 3(or 4)-methoxyphenoxyethyl, 4-fluoro(or

chloro)phenoxyethyl, 3(or 4)-methylphenoxyethyl, 2-carboxyethyl, 2-

methoxycarbonylethyl, 2-t-butoxycarbonylethyl, 2-methylcarbamoylethyl,

2-chloroethyl, chloromethyl, allyloxymethyl,

(2-ethoxyethoxy)methyl, benzyloxymethyl,

4-piperidinyloxymethyl, (N-t-butoxycarbonyl-4-piperidinyl)oxymethyl, 3(or

4)-pyridyloxymethyl, hydroxymethyl, 2-hydroxyethyl, acetoxymethyl,

1-acetoxyethyl, methylcarbamoyloxymethyl, 1-(N-methyl-N-

ethylcarbamoyloxy)methyl, (piperidino-carbonyloxy)methyl,

(benzylcarbamoyloxy)methyl,

(t-butoxycarbonylamino)methyl, aminomethyl,

1-aminoethyl, 1-(t-butoxycarbonylamino)ethyl,

2-aminoethyl, methoxycarbonylaminomethyl,

2-(methoxycarbonylamino)ethyl, ethoxycarbonylaminomethyl,

propoxycarbonylaminomethyl,

1-(fluorenylmethoxycarbonylamino)methyl,

2-(t-butoxycarbonylamino)ethyl,

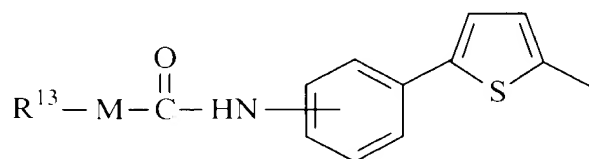
2-(fluorenylmethoxycarbonylamino)ethyl,

1-aminoisopropyl, 1-aminopropyl,

1-(t-butoxycarbonylamino)propyl,  
1-(t-butoxycarbonylamino)isopropyl,  
1,5-diaminopentyl, 1,5-bis(t-butoxycarbonylamino)-pentyl,  
methyaminomethyl, ethylaminomethyl,  
(N-methyl-N-ethylamino)methyl,  
dimethylaminomethyl, pentylaminomethyl,  
t-butylaminomethyl, methylaminoethyl,  
3-(2-(N-methyl-N-methoxycarbonylamino)methyl,  
1-(N-methyl-N-t-butoxycarbonylamino)methyl,  
1-(N-ethyl-N-t-butoxycarbonylamino)methyl,  
2-(N-methyl-N-(fluorenylmethoxycarbonyl)amino)-ethyl, 2-(N-methyl-N-(t-butoxycarbonyl)amino)ethyl, 1-(N-methyl-N-(dimethylcarbamoyl)amino)methyl,  
1-(dimethylcarbamoylamino)methyl,  
1-(N-(ethylcarbamoyl)amino)methyl,  
2-(N-(ethylcarbamoyl)amino)ethyl, benzoylaminomethyl, 2-benzoylaminoethyl, acetylaminomethyl, isobutyrylaminomethyl, pivaloylaminomethyl,  
1-(methanesulfonylamino)methyl,  
2-(methanesulfonylamino)ethyl, methoxyacetylaminomethyl, cyclopentylloxycarbonylaminomethyl,  
pyridylcarbonylaminomethyl, morpholinocarbonylaminomethyl, benzyloxycarbonylaminomethyl,  
1-(4-methoxyphenylsulfonylamino)methyl,

1-(2-hydroxyethylamino)methyl,  
 morpholinomethyl, 1-(2-oxo-1,3-oxazolidin-1-yl)methyl, 1-(2-oxopyrrolidin-1-yl)methyl,  
 1-(3,4,4-trimethylhydantoin-1-yl)methyl, allylaminomethyl, 1-(2-ethoxyethylamino)methyl,  
 benzylaminomethyl, 1-(3-pyridylmethylamino)methyl,  
 2-phenyl-1-aminoethyl, 1-amino-1-phenylmethyl,  
 1-t-butoxycarbonylamino-1-phenylmethyl,  
 1-amino-2-phenylethyl, 1-t-butoxycarbonylamino-2-phenylethyl, 1-amino-2-methoxyethyl,  
 1-t-butoxycarbonylamino-2-methoxyethyl, 1-amino-3-carboxypropyl, 1-t-butoxycarbonylamino-3-carboxypropyl, 1-amino-3-(t-butoxycarbonyl)propyl, 1-t-butoxycarbonylamino-3-t-butoxycarbonylpropyl, etc.), 1-amino-2-benzyloxyethyl,  
 1-t-butoxycarbonylamino-2-benzyloxyaminoethyl,  
 1-amino-2-(3-pyridyl)ethyl, 1-t-butoxycarbonylamino-2-(3-pyridyl)ethyl, 1-amino-2-(4-pyridyl)ethyl, 1-t-butoxycarbonylamino-2-(4-pyridyl)ethyl, 1-amino-2-hydroxyethyl,  
 1-t-butoxycarbonylamino-2-hydroxyethyl,  
 (1,5-diaminopentyl, 1-t-butoxycarbonylamino-5-aminopentyl, 1,5-bis(t-butoxycarbonylamino)pentyl, 1-amino-5-(t-butoxycarbonylamino)pentyl, 1-amino-2-cyclohexylethyl, 1-t-butoxycarbonylamino-2-cyclohexylethyl,

(c)

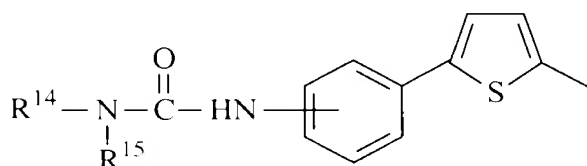


wherein

M=O and R<sup>13</sup> is methyl, ethyl, propyl, isopropyl, benzyl, 2-methoxyethyl, 2-chloroethyl, 2-aminoethyl, 2-phthalimidoethyl, allyl, phenyl, or

M=S and R<sup>13</sup> is methyl, ethyl,

(d)



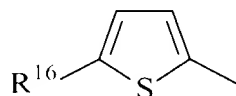
wherein

R<sup>15</sup> is hydrogen and

R<sup>14</sup> is hydrogen, methyl, ethyl, propyl, isopropyl, butyl, isobutyl, pentyl, hexyl, 1-naphthyl, 3(or 4)-chlorophenyl, 3-methoxyphenyl, allyl, cyclohexylmethyl, benzyl, 2-chloroethyl, methoxymethyl, 2-methoxyethyl, 2-hydroxyethyl, 2-((t-butyl)(diphenyl)silyloxy)ethyl, carboxymethyl, ethoxycarbonylmethyl, methylcarbamoylmethyl, or 3-pyridyl,

R<sup>14</sup> is ethyl and R<sup>15</sup> is methyl,

(e)



wherein

R<sup>16</sup> is 2-benzothienyl, 2-benzofuranyl, 2(or 3)-thienyl, 2-furyl, 3-pyridyl, 1-methyl-4-pyridyl, 6-methyl-3-pyridyl, 6-methoxy-3-pyridyl, 5-methoxycarbonylamino-3-pyridyl, 5-acetyl-2-thienyl, 2-methylcarbamoyl-5-benzofuranyl.

27. (New) A pharmaceutical composition which comprises the compound of Claim 18 or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier or excipient.

28. (New) A process for preparing a pharmaceutical composition which comprises admixing the compound of Claim 18 or a pharmaceutically acceptable salt thereof with a pharmaceutically acceptable carrier or excipient.

29. (New) A method for treating, reducing, arresting, or alleviating matrix metalloproteinases (MMP) or tumor necrosis factor  $\alpha$  (TNF  $\alpha$ )-mediated disease, the method comprising administering to a patient a therapeutically effective amount of the compound of Claim 18 or a pharmaceutically acceptable salt thereof.

30. (New) A method for inhibiting matrix metalloproteinases (MMP) or tumor necrosis factor  $\alpha$  (TNF  $\alpha$ ), the method comprising administering to a patient an effective amount of the compound of Claim 18 or a pharmaceutically acceptable salt thereof.

31. (New) A process for manufacturing a medicament, said process comprising contacting the compound of Claim 18 or a pharmaceutically acceptable salt thereof with a pharmaceutically acceptable carrier.